Cureus
Part of SPRINGER NATURE

Open Access Original Article

Rates of Diabetes Diagnoses and Diabetic Ketoacidosis Episodes Before Versus During the COVID-19 Pandemic

Review began 09/17/2026
Review ended 10/30/2026
Published 11/04/2026

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DOI: 10.7759/cureus.119131

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Abstract

Objectives

To determine whether the incidence of new-onset diabetes mellitus (DM) differed before and during the COVID-19 pandemic, and to compare the severity of diabetic ketoacidosis (DKA) at diagnosis. We hypothesized that DM incidence increased during the COVID-19 pandemic, with a corresponding rise in DKA severity.

Methods

We performed a retrospective analysis of youth (ages 0-18 years) newly diagnosed with DM at a single, free-standing children's hospital in Orlando, Florida. Patients diagnosed prior to the COVID-19 pandemic (September 2017-March 2020) were compared to those diagnosed during the COVID-19 pandemic (March 2020-September 2022). Outcomes included incidence of DM stratified by type (type 1 versus type 2), DKA rates and severity at diagnosis, and subgroup analyses by ethnicity and insurance status.

Results

The overall incidence of pediatric DM increased during the COVID-19 pandemic without a significant rise in DKA rates or severity. When stratified, only youth with type 2 diabetes showed a significantly higher incidence during the pandemic. Increases in DM diagnoses also were observed among non-privately insured youth and those of Hispanic background.

Conclusions

The COVID-19 pandemic was associated with higher rates of pediatric DM diagnoses, particularly among socioeconomically vulnerable populations without a corresponding increase in DKA severity. These findings suggest a shift in clinical presentation and highlight the disproportionate impact of the pandemic on disadvantaged groups. Further research is warranted to evaluate the long-term influence of COVID-19 on pediatric DM incidence and presentation.

Categories: Pediatrics, Infectious Disease, Endocrinology/Diabetes/Metabolism
Keywords: covid-19, diabetes, diabetic ketoacidosis, diagnosis rates, disease severity, pandemic, pediatrics

Introduction

Diabetes mellitus (DM) is a growing public health concern affecting millions of people in the United States, including about 210,000 children and adolescents under the age of 20 years [1]. Research conducted in the last decade has shown a steady increase in the incidence of type 1 diabetes (T1D) and type 2 diabetes (T2D) in pediatric populations, with over 23,000 children and adolescents diagnosed each year [1]. When diagnosis is delayed, serious complications such as diabetic ketoacidosis (DKA) may occur [2]. Children presenting in DKA at diagnosis have a higher risk of morbidity and mortality, necessitating increased medical costs and healthcare resource utilization such as intensive care unit-level care [3].

The Centers for Disease Control released a report describing a potential correlation between an increased incidence of both T1D and T2D diagnosis for individuals younger than 18 years of age and COVID-19 diagnosis [4]. Common initial symptoms of DM are polyuria, polydipsia, and significant weight loss. T1D is an autoimmune medical condition that leads to destruction of the body's pancreatic B-cells and eventual insulin deficiency. The true etiologic mechanism of T1D is not clearly understood; however, it is well-known that genetics, immunological factors, and environmental circumstances contribute greatly to the onset of this condition [1]. Viruses such as Coxsackievirus, rotavirus, mumps, and cytomegalovirus are known to be associated with the development of autoimmune conditions, including T1D [5]. Individuals with COVID-19

may experience hyperglycemia from stress, impaired glucose clearance, and dysregulated insulin homeostasis. Additionally, ex vivo studies have shown the SARS-CoV-2 virus can preferentially infect pancreatic beta islet cells, potentially accelerating apoptotic pathways [6]. If direct infection and lysis of beta islet cells is occurring, this could introduce autoantigens to an already-heightened immune system, leading to continued autoimmune islet cell damage known to be associated with T1D [6]. These concerns have prompted worldwide investigations into the relationship between DM and COVID-19. Recent literature from Australia and Saudi Arabia has illustrated an increase in the prevalence of T1D and severity of DKA presentation throughout the pandemic [7-9]. Increased DKA severity may reflect reluctance to seek care during the height of the pandemic due to infection risk.

T2D, on the other hand, results from insulin resistance, often related to lifestyle and genetic factors [2]. This increase in T2D could be attributed to a decrease in overall physical activity including reduced engagement in hobbies and sports, lack of in-person schooling, and other general activities amongst children because of the “stay-home” orders during the height of the pandemic. Pandemic-initiated global lockdowns also caused socioeconomic hardship for many and strained healthcare systems. This, in turn, limited accessibility to care and delayed the diagnosis of DM [10]. It is obvious multiple factors play a role in the relationships between the COVID-19 pandemic, diabetes, and DKA in the pediatric populations, but further clarification is needed from the scientific community.

In this study, we aimed to determine: 1) if there was a change in the rate of pediatric patients diagnosed with DM during the COVID-19 pandemic period (March 2020-September 2022) compared to an equivalent pre-pandemic period (September 2017-March 2020); 2) if there was a change in the rate and severity of DKA at DM diagnosis during the COVID-19 pandemic compared to the pre-pandemic period; and, 3) if the severity of DKA at DM diagnosis had an association with COVID-19-positive status (without establishing causality).

This article was previously presented as a meeting poster presentation at The Endocrine Society’s Annual Meeting on June 16, 2023, in Chicago, Illinois, and the Pediatric Endocrine Society's Annual Conference on May 3, 2024, Chicago, Illinois.

Materials And Methods

Data collection

This retrospective chart review used the children’s hospital’s electronic health records (EHR). Eligible patients included those with new-onset DM diagnosed in inpatient or outpatient settings.

Data from participants diagnosed with T1D and T2D between September 5, 2017, and September 1, 2022, were collected. Data included age, sex, race and ethnicity, insurance information, medical history (such as date of DM diagnosis, type of DM (T1D or T2D), and DKA diagnosis), family history of DM, and initial laboratory studies at presentation (such as blood glucose, pH, bicarbonate, hemoglobin A1c, COVID-19 status, as well as COVID-19 known exposures). Most youth admitted to the hospital were tested for COVID-19 infection during the pandemic using the Xpert Xpress SARS-CoV-2/Flu/RSV nasopharyngeal swab test (Cepheid Inc., Sunnyvale, US).

DKA at presentation was identified based on the documented diagnosis in the medical record. The 2018 International Society for Pediatric and Adolescent Diabetes (ISPAD) guidelines were used to classify the severity of DKA [11]. The classification utilized the following parameters to categorize DKA presentation in addition to a hyperglycemic state of blood glucose over 200mg/dL: mild DKA (venous pH <7.3 or bicarbonate 10 to <15 mmol/l), moderate DKA (venous pH <7.2 or bicarbonate 5 to 9 mmol/l), and severe DKA (venous pH <7.1 or bicarbonate <5 mmol/l) [11]. When venous pH and serum bicarbonate corresponded to different DKA severity categories, the more severe category was assigned. For some patients, particularly those transferred from outside hospitals, initial laboratory values were unavailable despite a documented diagnosis of DKA. These patients were included in the overall DKA frequency analysis but excluded from the severity classification when sufficient laboratory data were unavailable.

The data were stratified into two time periods: two years and five months before the pandemic to its start (09/05/2017-03/01/2020) and two years and five months during the pandemic to its end (03/02/2020-09/01/2022). Both these time-period datasets were analyzed for the prevalence of DM and severity of DKA in those who presented with DKA at the time of diabetes diagnosis. We compared this information between the two time periods. Additionally, we assessed COVID-19 positivity rates among those with new-onset DM during the pandemic and determined if there was a correlation between COVID-19 status and DKA severity. Finally, we stratified the data based on the type of diabetes to determine if there were any differences between T1D and T2D.

Statistical analysis

Statistical analyses compared two groups on demographic variables and DM characteristics: those diagnosed with DM during the pre-pandemic period and those diagnosed with DM during the pandemic-era period.

These periods were defined pragmatically based on the timing of widespread pandemic-related disruptions to healthcare access, daily routines, and clinical operations at our institution, rather than as precise markers of SARS-CoV-2 transmission. The pandemic-era period was defined as March 2020 through the initiation of the study, corresponding to changes in healthcare utilization, school attendance, and health-seeking behavior. The pre-pandemic period comprised the immediately preceding interval of equivalent duration. While SARS-CoV-2 transmission likely occurred outside these boundaries, this operational definition allowed for comparison of DM presentation before versus during a period of substantial system-level and society disruption.

Comparisons between groups were exploratory and descriptive in nature. A chi-square test analyzed categorical variables, including sex distribution, type of insurance, type of DM, and the proportion of youth with different DM-related complications. A Mann-Whitney U test compared the age distribution between the pre-pandemic group and the pandemic era group, considering the non-normally distributed age data. A one-proportion test assessed whether there was a significant difference in the proportion of newly diagnosed DM cases during the COVID-19 pandemic compared to before the pandemic. Given the limited sample size, initial analyses included all newly diagnosed diabetes cases (T1D and T2D); diabetes type-specific findings are reported descriptively where relevant.

All statistical analyses were performed using IBM SPSS Statistics for Windows, Version 28 (Released 2021; IBM Corp., Armonk, New York, United States). The results were considered statistically significant at a two-tailed P-value of less than 0.05.

Results

A total of 509 participants were diagnosed with T1D or T2D at our institution between September 5, 2017, and September 1, 2022 (214 in the pre-pandemic period and 295 during the pandemic-era period). The characteristics of the study population are described in Table *1*.

Variable/Demographics		Pre-pandemic period (09/05/2017-03/01/2020)	Pandemic period (03/02/2020-09/01/2022)	P-value
		M (SD)	M (SD)	
Age (years)		10.5 (4.2)	11.2 (4.1)	0.070
Hemoglobin A1C (%)		11.4 (2.3)	11.3 (2.5)	0.439
		N (%)	N (%)	
Sex	Female	100 (47)	144 (49)	0.642
	Male	114 (53)	151 (51)	
Ethnicity	Non-Hispanic or Latino	132 (62)	156 (53)	0.007*[b]
	Hispanic or Latino	82 (38)	129 (44)	
	Not available	0 (0)	10 (3)	
Insurance Status	Medicaid	117 (55)	190 (64)	0.027*[c]
	Private Insurance	97 (45)	105 (36)	
Race	Black or African American	42 (20)	57 (19)	0.100
	White or Caucasian	110 (51)	127 (43)	
	Other/Unknown/Declined to answer	62 (29)	111 (38)	
Diabetes type	Type 1	171 (80)	187 (63)	0.398
	Type 2	43 (20)	108 (37)	0.000*[d]
DKA[a] severity	Mild	25 (33)	32 (39)	0.179
	Moderate	31 (40)	20 (24)	
	Severe	21 (27)	30 (37)	
COVID-19 status	Positive	0 (0)	23 (8)	N/A

TABLE 1: Demographic data of the study participants

[a]DKA, diabetic ketoacidosis; [b]Ethnicity $\chi2(2,509) = 9.828$; [c]Insurance Status $\chi2(1,509) = 4.909$; [d]Diabetes Type 2 $\chi2(1,509) = 16.216$; *$p<0.05$ (statistically significant).

Note: DKA frequency includes all patients with a documented diagnosis of DKA at presentation. Severity classification was limited to patients with sufficient initial laboratory data (pH and/or bicarbonate). Therefore, the number of patients with classified DKA severity is lower than the total number of documented DKA cases.

A greater proportion of newly diagnosed DM cases occurred during the pandemic-era period (n=295, 58.0%) compared to the pre-pandemic period (n=214, 42.0%; P<0.001). Exploratory comparisons of demographic characteristics across the two periods identified differences in the distribution of ethnicity and insurance type. Specifically, a higher proportion of newly diagnosed DM cases during the pandemic-era period occurred among Hispanic youth (P=0.007) and among youth insured by Medicaid (P=0.027). However, there were no differences in DM diagnosis based on sex, race, or age between the two periods.

In contrast, we did not find any significant differences in the severity levels of DKA among participants diagnosed before and during the pandemic (P=0.179). We also did not find a significant difference in DKA severity levels among youth who tested positive versus negative for COVID-19 at diagnosis (P=0.867).

Next, we looked at differences in rates of new-onset DM and DKA diagnoses by diabetes type. Among youth diagnosed with T1D, there were no statistically significant differences in the number of new-onset diagnoses before (n=171, 47.8%) versus during (n=187, 52.2%) the pandemic (P=0.398). There also were no statistically significant differences in the number of DKA diagnoses among youth with T1D before (n=77; 45.0%) versus during (n=87; 46.5%) the pandemic (P=0.777). Among participants diagnosed with T2D, a

significantly greater number were diagnosed during the pandemic (n=108, 71.5%) compared to before the pandemic (n=43, 28.5%; P<0.001). However, significantly fewer youth with new-onset T2D presented with DKA during the pandemic (n=5, 4.6%) compared to the pre-COVID period (n=8, 18.6%; P=0.006). The results discussed above are presented in Figure *1*.

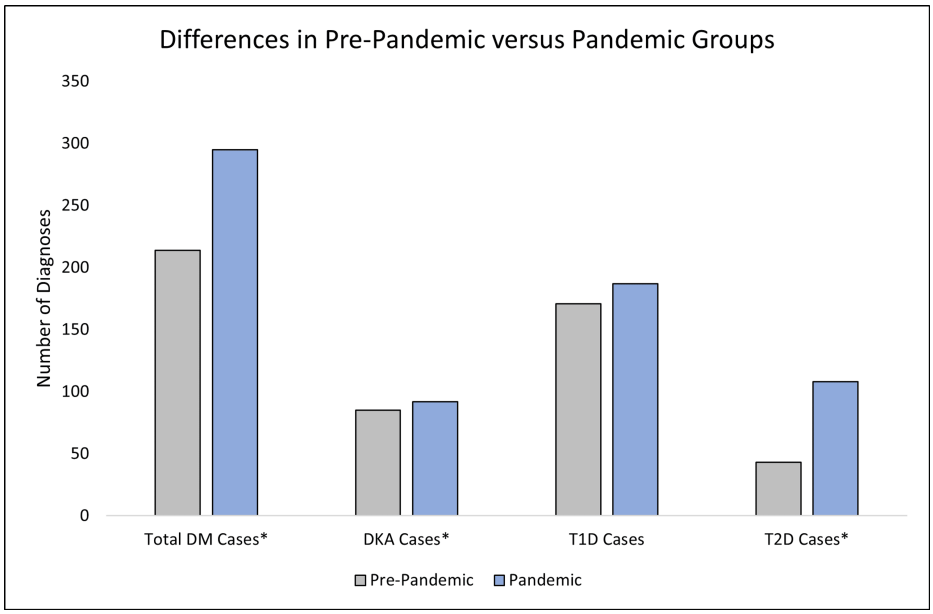


FIGURE 1: Number of overall new-onset DM, DKA, T1D, and T2D

Diagnoses made before (09/05/2017-03/01/2020) and during the pandemic (03/02/2020-09/01/2022); *P<0.05 is statistically significant.

DM, diabetes mellitus; DKA, diabetic ketoacidosis; T1D, type 1 diabetes; T2D, type 2 diabetes.

Discussion

This retrospective study analyzed changes in the incidence and severity of pediatric DM presentation during the COVID-19 pandemic compared to before the pandemic at a single, free-standing children's hospital. We found that among 509 youth diagnosed with DM between September 2017 and September 2022 at our institution, a significantly greater number of DM diagnoses were made after the start of the pandemic (between March 2020 and September 2022). Before the pandemic, 171 children (47.8%) were diagnosed with T1D in a two-year and five-month period compared to 187 children (52.2%) during the two-year and five-month period of the pandemic. While 43 children (28.5%) were diagnosed with T2D pre-pandemic, a substantially greater number (n=108; 71.5%) were diagnosed during an equal length of time during the pandemic (P<0.001). A disproportionate increase in T2D diagnoses during the pandemic indicates that factors beyond the impact of COVID-19 on autoimmune function may be at play. Lifestyle changes due to quarantine lockdowns and "stay-at-home" orders are commonly cited as a major driver for the increased T2D prevalence [1].

Also, literature indicates that the development of insulin resistance could be a direct effect of COVID-19 infection [12,13]. Several studies have reported hyperglycemia as a frequent finding in adults following COVID-19 diagnosis [12,13]. Meanwhile, Keiner and colleagues discovered that youth with COVID-19 who develop DKA require significantly higher insulin doses compared to their peers without COVID-19 infection, suggesting possible insulin resistance from the viral infection itself [14]. In our study, COVID-19-positive youth (n=23) comprised a small proportion of the new DM diagnoses (n=295) during the pandemic, despite significant changes in incidence of DM diagnosis between groups. A large portion of diagnoses made during the pandemic had an unknown COVID-19 status (n=157); therefore, it is unclear what percentage of our new-onset DM population were truly COVID-19-positive during the pandemic.

Several international studies demonstrated the increase in DM and DKA incidence in children during the pandemic. However, conflicting results have been noted concerning the incidence of DM and DKA severity at diagnosis. A retrospective study of 260 Saudi Arabian children in 2019-2020 determined an increase in the prevalence of T1D without an increase in DKA severity during the pandemic period [9]. On the contrary, a meta-analysis reviewing 26 studies published on this topic worldwide reported an increase in new-onset T1D diagnoses as well as an increase in prevalence of DKA and DKA severity in 2020 compared to 2019 [15]. Our retrospective study found a significant increase in the prevalence of DM at diagnosis during the pandemic, with no significant change in the rate or severity of DKA. For youth with T1D, while there were

more DKA episodes during the pandemic (n=87) compared to pre-COVID (n=77), the increase was not statistically significant. This could be because the difference was not sizeable to confidently exclude random variation's influence, or the sample size did not provide enough power for the test. In contrast, the number of DKA episodes in youth with T2D was small overall, and during COVID there were fewer DKA episodes (n=5) compared to pre-COVID (n=8). Even though the numbers decreased, and the difference was statistically significant, small sample sizes can make these tests less reliable and sensitive to small changes. The overall significant difference in DKA episodes may be due to the larger combined sample, while the separate tests for T1D and T2D were affected by the distribution of cases and smaller sample sizes. The conflicting findings on this topic when comparing previously published studies could be attributed to the variance in heterogenicity of the populations studied, prevalence of COVID-19 in the region, and time periods of data collection.

Our study explored correlations among race and ethnicity, age, sex, and insurance status in children diagnosed with DM. Significantly higher rates of new-onset DM were observed in Hispanic or Latino children during the pandemic (n=129 diagnoses) compared to pre-pandemic (n=82 diagnoses), representing a 57% increase (P=0.007). Additionally, significantly higher rates of new-onset DM also were observed in children insured with Medicaid (n=117 diagnoses) compared to before the pandemic (n=73 diagnoses), representing a 62% increase (P=0.027). We observed significant differences in the proportions of Hispanic and Medicaid-insured patients between the pre-pandemic and pandemic periods. However, potential confounding between ethnicity and insurance status limits interpretation of these findings. Future studies incorporating multivariable analyses are needed to clarify these associations. The observed rise in DM diagnoses among various ethnic and insurance groups highlights the potential impact of social determinants of health such as poverty and ethnicity on the health outcomes of vulnerable populations during the pandemic. These disparities are well-documented in the literature even before the COVID-19 pandemic. Studies have shown a rising prevalence of obesity among adolescents of non-White ethnicities over nearly two decades [16]. Additionally, within this demographic, individuals with T1D or T2D with government insurance had higher HbA1c values compared to their privately insured counterparts [17]. While these disparities were evident before the pandemic, subsequent research has shown an exacerbation of negative health outcomes among marginalized populations. Studies in the United Kingdom and the United States have revealed persistence in low attainment of diabetes care throughout the pandemic and an increased risk of hospitalization and mortality from COVID-19 in non-White ethnicities [18,19]. These studies were completed mostly in adult populations, and similar outcomes can be expected amongst children and adolescents living in impoverished households. However, future studies should be conducted to demonstrate trends among youth of varying ethnicities and economic backgrounds.

Limitations

Due to the retrospective nature of this study, there was missing data, especially on COVID-19-positive status; therefore, we could not conclude whether the viral infection directly influenced the increase in DM and DKA prevalence. Due to the lack of a population denominator, true incidence of COVID-19 and DM diagnoses cannot be established, and causality cannot be concluded. The small sample size of COVID-positive patients is another possible disadvantage and limits the study's power. The COVID-19 testing used by our hospital and outside hospitals may have differed from one another, and may not be available in other settings. Additionally, the data is available from a single center, a free-standing children's hospital, which may not be applicable when data is extrapolated to other settings. The study may also be affected by biases, including selection and referral biases. In general, patients were less likely to seek healthcare during the pandemic, and this confounder was not explored in detail in our analysis. Other confounding factors in the data include, BMI, family history, lifestyle factors, and direct socioeconomic measures, were not assessed. Nonetheless, these data are a valuable contribution to the existing literature regarding pediatric DM, especially in the face of COVID-19.

Conclusions

This retrospective study's findings demonstrate an increase in the rate of pediatric patients diagnosed with DM during the COVID-19 pandemic compared to an equal length of time before the pandemic. A substantial increase in new-onset T2D was noted during the pandemic. Additionally, we saw a significantly skewed impact of this increased DM diagnosis on children from ethnic and marginalized backgrounds. Due to the study's limitations, we cannot establish true population-level incidence of DM or infer causality between the SARS-CoV-2 infection and DM. However, our study's findings support the current narrative surrounding the pandemic regarding the immense socioeconomic stress of a global health crisis on the healthcare system and the U.S. population. The influence of the SARS-CoV-2 infection, changes in lifestyle during the pandemic, limited healthcare access, and socioeconomic factors should all be considered as possible explanations of increased prevalence of pediatric DM worldwide, though the influence and causality of each factor remain unknown. Future research should investigate biochemical and immunological aspects of children with DM who contracted COVID-19 before DM diagnosis to provide more tailored insights into the pandemic's effects on physiological processes and potential pathological changes resulting in DM.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Shilpa Gurnurkar, Adrien Thokalath, Sweta Chalise, Felicia Cooper, Jessica Pierce

Acquisition, analysis, or interpretation of data: Shilpa Gurnurkar, Adrien Thokalath, Sweta Chalise, Felicia Cooper, Jessica Pierce

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Disclosures

Human subjects: Informed consent for treatment and open access publication was obtained or waived by all participants in this study. Nemours Children's Health Institutional Review Board issued approval 1912116. **Animal subjects:** All authors have confirmed that this study did not involve animal subjects or tissue. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

Acknowledgements

The authors acknowledge the assistance of Editorial Services of Nemours Children’s Health.

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